


# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>LU6078/CB</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/EP 03/14358</b>	International filing date ( <i>day/month/year</i> ) <b>17.12.2003</b>	Priority date ( <i>day/month/year</i> ) <b>19.12.2002</b>
International Patent Classification (IPC) or both national classification and IPC <b>C07D333/22</b>		
Applicant <b>BASELL POLYOLEFINE GMBH et al.</b>		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 2 sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the opinion</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>		
Date of submission of the demand  <b>28.06.2004</b>	Date of completion of this report  <b>05.04.2005</b>	
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 eprmu d Fax: +49 89 2399 - 4465	Authorized Officer  <b>Bakboord, J</b>  Telephone No. +49 89 2399-2168	



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP 03/14358

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-13 as originally filed

**Claims, Numbers**

1-8 received on 13.10.2004 with letter of 12.10.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
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International application No. **PCT/EP 03/14358**

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	1-8
	No: Claims	
Inventive step (IS)	Yes: Claims	1-8
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-8
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**V Reasoned statement under Art 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

V.1 The present invention relates to a process for preparing heterocyclic ketones by reacting a heterocyclic compound with an  $\alpha,\beta$ -unsaturated carboxylic acid or its anhydride in a mixture of a solution of at least one strong organic acid and at least one water absorbent.

V.2 Reference is made to the following documents:

- D1: RYABOV A N ET AL: 'ZIRCONIUM COMPLEXES WITH CYCLOPENTADIENYL LIGANDS INVOLVING FUSED A THIOPHENE FRAGMENT' ORGANOMETALLICS, ACS, COLUMBUS, OH, US, vol. 21, no. 14, 2002, pages 2842-2855, XP001106373 ISSN: 0276-7333 cited in the application
- D2: EWEN J A ET AL: 'Chiral Ansa Metallocenes with Cp Ring-Fused to Thiophenes and Pyrroles: Syntheses, Crystal Structures, and Isotactic Polypropylene Catalysts' JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, US, vol. 123, 2001, pages 4763-4773, XP002233282 ISSN: 0002-7863 cited in the application
- D3: BINDER D ET AL: 'A facile route to functionalized cyclopenta[b]thiophenones based on the structure of the selective cox-2 inhibitor flosulide' MONATSHFTE FÜR CHEMIE, vol. 129, 1998, pages 887-896, XP002278577 Austria
- D4: BERGMAN J ET AL: 'intramolecular ring closure of alpha, beta-unsaturated 3-acylindoles' TETRAHEDRON LETTERS, vol. 28, no. 32, 1987, pages 3741-3744, XP002278578 GB

**V.3 Novelty**

Document D1 discloses the synthesis of cyclopenta[b]benzothiophene by adding a benzothiophene to a mixture of a solution of phosphorus pentoxide in methane sulphonic acid and methacrylic acid at rt (Scheme 4, and page 2852 first column, first paragraph).

Document D2 discloses the synthesis of a sulfur containing cyclic ketosystem by reaction of a substituted thiophene with methacrylic acid in the presence of super-

polyphosphonic acid.

Document D3 discloses the synthesis of cyclopenta[b]thiophenones through a friedel crafts reaction (page 889, first paragraph, scheme 2).

Document D4 discloses the synthesis of cyclopent[b]indoles by reacting an indole Grignard reagent with substituted acryloyl chlorides (Scheme 1).

A process for the synthesis of heterocyclic ketosystems by adding a substituted heterocyclic compound together with an  $\alpha,\beta$ -unsaturated carboxylic acid to a mixture of a solution of at least one strong organic acid and at least one water absorbent, whereby the reaction is performed at 50 to 110°C is disclosed in none of the documents. Claims 1-9 therefore fulfill the requirements of Art 33(2) PCT.

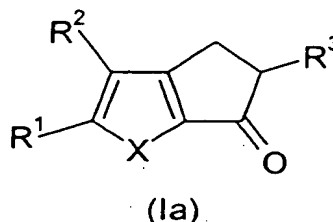
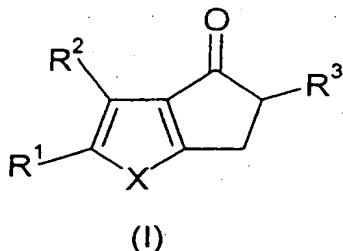
#### V.4 Inventive step

Starting from document D1 the problem to be solved by the present application may be regarded as how to provide a novel possibly improved process for the synthesis of heterocyclic ketones. The solution of the applicant resides in adding the substituted heterocyclic compound **together** with the  $\alpha,\beta$ -unsaturated carboxylic acid to a mixture of a solution of at least one strong organic acid and at least one water absorbent, rather than adding the substituted hetero cycle to a mixture of a solution of at least one strong organic acid and at least one water absorbent **and** the  $\alpha,\beta$ -unsaturated carboxylic acid and performing the reaction at 50 to 110°C rather than at rt.

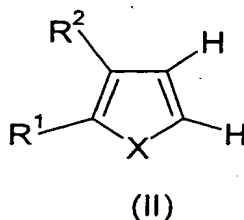
The result of these two modifications to the process of document D1 is that the yield of the reaction is increased by 10%. As the modifications made to the process of D1 have not been made obvious by the teaching of document D1, the solution of the applicant may be regarded as involving an inventive step (Art 33(3) PCT).

We claim:

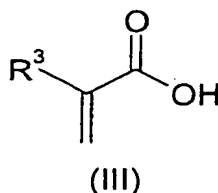
1. A process for preparing heterocyclic ketones of the formulae (I) or (Ia)



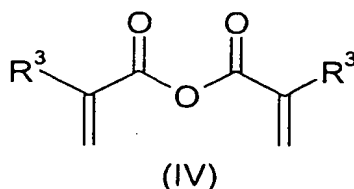
by reacting a heterocyclic compound of the formula (II)



with an  $\alpha,\beta$ -unsaturated carboxylic acid of the formula (III)



or with its anhydride of the formula (IV)



which comprises performing the reaction in a liquid reaction medium which comprises at least one strong organic acid and at least one water absorbent, where the strong organic acid has a higher acid strength than the carboxylic acid of the formula (III) by adding simultaneously the heterocyclic compound of the formula (II) together with the  $\alpha,\beta$ -unsaturated carboxylic acid of the formula (III) or together with its anhydride of the formula (IV) to said liquid reaction medium, wherein the reaction is carried out in the temperature range from 50 to 110°C, and

where

R<sup>1</sup> is hydrogen or a C<sub>1</sub>-C<sub>40</sub> carbon-containing group,

R<sup>2</sup> is hydrogen or a C<sub>1</sub>-C<sub>40</sub> carbon-containing group, or

R<sup>1</sup> and R<sup>2</sup> together form a cyclic ring system,

R<sup>3</sup> is a C<sub>1</sub>-C<sub>40</sub> carbon-containing group and

X is an element of the 16th group of the Periodic Table or is a divalent nitrogen group -(N-R<sup>4</sup>)-, where R<sup>4</sup> is an electron-withdrawing radical which is selected from the group consisting of perhalogenated C<sub>1</sub>-C<sub>40</sub> carbon-containing radicals and C<sub>1</sub>-C<sub>40</sub> organosulfonyl groups.

2. A process as claimed in claim 1, wherein X is sulfur.

3. A process as claimed in claim 1 or 2, wherein the strong organic acid is a C<sub>1</sub>-C<sub>8</sub>-alkylsulfonic acid.

4. A process as claimed in any of claims 1 to 3, wherein the water absorbent is phosphorus pentoxide.

5. A process as claimed in any of claims 1 to 4, wherein at least 50% by weight of the liquid reaction medium consists of a mixture of methanesulfonic acid and phosphorus pentoxide.

6. A process as claimed in any of claims 1 to 5, wherein the molar ratio of the heterocyclic compound of the formula (II) to the  $\alpha,\beta$ -unsaturated carboxylic acid of the formula (III) is in the range from 5 : 1 to 1 : 100.

7. A process as claimed in any of claims 1 to 6, wherein the mass ratio of the heterocyclic compound of the formula (II) to the liquid reaction medium is in the range from 1 : 2 to 1 : 1000.

8. A process as claimed in any of claims 1 to 7, wherein the mass ratio of the water absorbent to the strong organic acid is in the range from 1 : 99 to 25 : 75.